

In re: Ekwuribe et al.  
Serial No.: 09/873,757  
Filed: June 4, 2001  
Page 2 of 9

**In the Claims**

The following list of claims will replace all prior versions and listings of claims in the Application. Please amend the claims as follows.

1-102. (Canceled)

103. (Previously Presented) A mixture of conjugates each comprising a human growth hormone drug coupled to an oligomer that comprises a polyalkylene glycol moiety and a lipophilic moiety that comprises one or more linear, saturated or unsaturated alkyl moieties having 1 to 28 carbon atoms, said mixture having a molecular weight distribution with a standard deviation of less than about 22 Daltons.

104. (Previously Presented) The mixture of claim 103, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated alkyl moieties having 2 to 12 carbon atoms.

105. (Previously Presented) The mixture of claim 103, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated alkyl moieties having 4, 5 or 6 carbon atoms.

106. (Previously Presented) A method of treating human growth hormone deficiency in a subject in need of such treatment, said method comprising:

administering an effective amount of a mixture of conjugates, each comprising a human growth hormone drug coupled to an oligomer that comprises a polyalkylene glycol moiety and a lipophilic moiety that comprises one or more linear, saturated or unsaturated alkyl moieties having 1 to 28 carbon atoms, said mixture having a molecular weight distribution with a standard deviation of less than about 22 Daltons, to the subject to treat the human growth hormone deficiency.

107. (Previously Presented) The method of claim 106, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated alkyl moieties having 2 to 12 carbon atoms.

In re: Ekwuribe et al.  
Serial No.: 09/873,757  
Filed: June 4, 2001  
Page 3 of 9

108. (Previously Presented) The method of claim 106, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated natural fatty acid moieties having 4, 5 or 6 carbon atoms.

109. (Previously Presented) A method of accelerating the growth rate of a human subject, said method comprising:

administering to the human subject a mixture of conjugates each comprising a human growth hormone drug coupled to an oligomer that comprises a polyalkylene glycol moiety and a lipophilic moiety that comprises one or more linear, saturated or unsaturated alkyl moieties having 1 to 28 carbon atoms, said mixture having a molecular weight distribution with a standard deviation of less than about 22 Daltons, in an amount sufficient to accelerate the human subject's growth rate.

110. (Previously Presented) The method of claim 109, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated alkyl moieties having 2 to 12 carbon atoms.

111. (Previously Presented) The method of claim 109, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated natural fatty acid moieties having 4, 5 or 6 carbon atoms.

112. (Previously Presented) A substantially monodispersed mixture of conjugates, each conjugate comprising a human growth hormone drug coupled to an oligomer that comprises a polyalkylene glycol moiety and a lipophilic moiety that comprises one or more linear, saturated or unsaturated alkyl moieties having 1 to 28 carbon atoms.

113. (Previously Presented) The mixture of claim 112, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated alkyl moieties having 2 to 12 carbon atoms.

In re: Ekwuribe et al.  
 Serial No.: 09/873,757  
 Filed: June 4, 2001  
 Page 4 of 9

114. (Previously Presented) The mixture of claim 112, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated natural fatty acid moieties having 2 to 18 carbon atoms.

115. (Previously Presented) A mixture of conjugates each comprising a human growth hormone drug coupled to a polymer having a polyalkylene glycol moiety and a lipophilic moiety that comprises one or more linear, saturated or unsaturated alkyl moieties having 1 to 28 carbon atoms, wherein the mixture has a dispersity coefficient (DC) greater than 10,000 where

$$DC = \frac{\left( \sum_{i=1}^n N_i M_i \right)^2}{\sum_{i=1}^n N_i M_i^2 \sum_{i=1}^n N_i - \left( \sum_{i=1}^n N_i M_i \right)^2}$$

wherein:

n is the number of different molecules in the sample;

$N_i$  is the number of  $i^{\text{th}}$  molecules in the sample; and

$M_i$  is the mass of the  $i^{\text{th}}$  molecule.

116. (Previously Presented) The mixture of claim 115, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated alkyl moieties having 2 to 12 carbon atoms.

117. (Previously Presented) A mixture of conjugates each comprising a human growth hormone drug coupled to a polymer having a polyalkylene glycol moiety and a lipophilic moiety that comprises natural fatty acid moieties having 4, 5 or 6 carbon atoms, wherein the mixture has a dispersity coefficient (DC) greater than 10,000 where

$$DC = \frac{\left( \sum_{i=1}^n N_i M_i \right)^2}{\sum_{i=1}^n N_i M_i^2 \sum_{i=1}^n N_i - \left( \sum_{i=1}^n N_i M_i \right)^2}$$

wherein:

n is the number of different molecules in the sample;

In re: Ekwuribe et al.  
Serial No.: 09/873,757  
Filed: June 4, 2001  
Page 5 of 9

$N_i$  is the number of  $i^{\text{th}}$  molecules in the sample; and  
 $M_i$  is the mass of the  $i^{\text{th}}$  molecule.

118. (Previously Presented) The mixture of claim 117, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated alkyl moieties having 1 to 28 carbon atoms.

119. (Previously Presented) The mixture of claim 117, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated alkyl moieties having 2 to 12 carbon atoms.

120. (Previously Presented) A mixture of conjugates in which each conjugate:

- (a) comprises a human growth hormone drug coupled to an oligomer comprising a polyalkylene glycol and a lipophilic moiety that comprises one or more linear, saturated or unsaturated alkyl moieties having 1 to 28 carbon atoms; and
- (b) has the same number of polyalkylene glycol subunits.

121. (Previously Presented) The mixture of claim 120, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated alkyl moieties having 2 to 12 carbon atoms.

122. (Previously Presented) The method of claim 120, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated natural fatty acid moieties having 4, 5 or 6 carbon atoms.

123. (New) A method of treating human growth hormone deficiency in a subject in need of such treatment, said method comprising:

administering an effective amount of a mixture of conjugates, each comprising a human growth hormone drug coupled to an oligomer that comprises a polyalkylene glycol moiety and a lipophilic moiety that comprises one or more linear, saturated or unsaturated natural fatty acid moieties having 4, 5 or 6 carbon atoms, said mixture having a molecular

In re: Ekwuribe et al.  
Serial No.: 09/873,757  
Filed: June 4, 2001  
Page 6 of 9

weight distribution with a standard deviation of less than about 22 Daltons, to the subject to treat the human growth hormone deficiency.

124. (New) The method of claim 123, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated alkyl moieties having 2 to 12 carbon atoms.

125. (New) A method of accelerating the growth rate of a human subject, said method comprising:

administering to the human subject a mixture of conjugates each comprising a human growth hormone drug coupled to an oligomer that comprises a polyalkylene glycol moiety and a lipophilic moiety that comprises one or more linear, saturated or unsaturated natural fatty acid moieties having 4, 5 or 6 carbon atoms, said mixture having a molecular weight distribution with a standard deviation of less than about 22 Daltons, in an amount sufficient to accelerate the human subject's growth rate.

126. (New) The method of claim 125, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated alkyl moieties having 2 to 12 carbon atoms.

127. (New) A substantially monodispersed mixture of conjugates, each conjugate comprising a human growth hormone drug coupled to an oligomer that comprises a polyalkylene glycol moiety and a lipophilic moiety that comprises one or more linear, saturated or unsaturated natural fatty acid moieties having 4, 5 or 6 carbon atoms.

128. (New) The mixture of claim 127, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated alkyl moieties having 1 to 28 carbon atoms.

129. (New) The mixture of claim 127, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated alkyl moieties having 2 to 12 carbon atoms.

130. (New) A mixture of conjugates each comprising a human growth hormone drug coupled to a polymer having a polyalkylene glycol moiety and a lipophilic moiety that comprises one or more linear, saturated or unsaturated natural fatty acid moieties having 4, 5

In re: Ekwuribe et al.  
Serial No.: 09/873,757  
Filed: June 4, 2001  
Page 7 of 9

or 6 carbon atoms, wherein the mixture has a dispersity coefficient (DC) greater than 10,000 where

$$DC = \frac{\left( \sum_{i=1}^n N_i M_i \right)^2}{\sum_{i=1}^n N_i M_i^2 \sum_{i=1}^n N_i - \left( \sum_{i=1}^n N_i M_i \right)^2}$$

wherein:

n is the number of different molecules in the sample;

$N_i$  is the number of  $i^{\text{th}}$  molecules in the sample; and

$M_i$  is the mass of the  $i^{\text{th}}$  molecule.

131. (New) The mixture of claim 130, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated alkyl moieties having 1 to 28 carbon atoms.

132. (New) The mixture of claim 130, wherein the lipophilic moiety comprises one or more linear, saturated or unsaturated alkyl moieties having 2 to 12 carbon atoms.

133. (New) A mixture of conjugates in which each conjugate:

(a) comprises a human growth hormone drug coupled to an oligomer comprising a polyalkylene glycol and a lipophilic moiety that comprises one or more linear, saturated or unsaturated natural fatty acid moieties having 4, 5 or 6 carbon atoms; and

(b) has the same number of polyalkylene glycol subunits.